which Notch resolves mixed neural identities by repressing an undesired genetic program.

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Program/Abstract # 217
Notch signaling has differing effects on subpopulations of retinal progenitor cells in zebrafish retinal development
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Cell-to-cell interactions mediated by the *Notch* pathway play critical roles in regulating the temporal pattern of neurogenesis. In the vertebrate retina, upon binding a ligand encoded by the *DSL* (*Delta/Serrate/lag-2*) genes, Notch signaling suppresses neuronal differentiation and promotes continued proliferation. Inhibition of Notch signaling results in an increase in the number of neuroblasts that differentiate as ganglion cells and cone photoreceptors, two early cell fates. Conversely, overexpression of a constitutively active form of Notch (NICD) promotes Muller glial differentiation, a later cell fate. Here we tested for a coordinated role of Notch in zebrafish retinal progenitor cell proliferation and subsequent differentiation using the *mindbomb* allele (*mib*^{ta52b}), which lacks Notch function, and two heat-shock transgenic lines that allow for temporal regulation of Notch signaling. In *mib* mutant embryos, BrdU and PH3 labeling revealed that in the absence of Notch signaling, a subset of retinal progenitor cells exits the cell cycle early and differentiates as ganglion cells, while the remainder of progenitor cells continues to proliferate in a spatial and temporal pattern similar to the wild-type pattern. Temporal expression of the NICD resulted in increased Muller glia differentiation at all time points tested as has been previously demonstrated, though mitotic cell numbers were not in excess of their wild-type siblings. Taken together, these data suggest that Notch signaling has differing effects on subpopulations of retinal progenitor cells in zebrafish retinal development.

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Program/Abstract # 218
Lots-of-rods (*lor*) regulates photoreceptor subtype specification in zebrafish
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The number and distribution of neurons generated during development of the vertebrate retina are tightly regulated and critical for image formation. This arrangement is particularly apparent in the highly ordered, crystalline-like mosaic of the photoreceptors in the teleost. Using as a model the mosaic pattern of photoreceptors in the zebrafish, we have undertaken a genetic screen to identify loci that are essential for photoreceptor subtype specification. We identified the locus, *lot-of-rods* (*lor*), that when mutated results in an increased number of rods and a reduced number of ultraviolet-sensitive (UV) cones in larvae and adults. This phenotype is the opposite of that observed in enhanced S-cone syndrome and the rd7 mouse. Quantitative and spatial pattern analyses suggest an approximate one-to-one exchange of rods for UV cones in the mutant compared to wild-type larvae with little alterations in red, green or blue cones. Linkage analysis and complementation testing indicate that the *lor* locus encodes a T-box transcription factor. In genetic chimeras, *lor* mutant cells failed to generate UV cones in a wild-type host. Conversely, wild-type cells displayed the capacity to differentiate into UV cones when transplanted into a mutant host. The identification of a novel function for a T-box gene in photoreceptor development provides a much needed system to understand the molecular network regulating neuronal subtype specification in the retina and dissect the UV vision pathway in a vertebrate. Supported by R1EY017753.

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Program/Abstract # 219
Intra-endodermal interactions are required for pancreatic β-cell induction
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The cellular origin of signals that regulate pancreatic β-cell induction is not clearly defined. Here, we investigate the seeming paradox that Hedgehog/Smoothened signaling functions during gastrulation to promote pancreatic β-cell development in zebrafish, yet has an inhibitory role during later stages of pancreas development in amniotes. Our cell transplantation experiments reveal that in zebrafish, Smoothened function is not required in β-cell precursors. At early somitogenesis stages, when the zebrafish endoderm first forms a sheet, pancreatic β-cell precursors lie closest to the midline; however, the requirement for Smoothened lies in their lateral neighbors, which ultimately give rise to the exocrine pancreas and intestine. Thus, pancreatic β-cell induction requires Smoothened function cell non-autonomously during gastrulation, to allow subsequent intra-endodermal interactions. These results clarify the function of Hedgehog signaling in pancreas development, identify an unexpected cellular source of factors that regulate β-cell specification, and uncover complex patterning and signaling interactions within the endoderm.

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Program/Abstract # 220
PAR-1 phosphorylates the ubiquitin ligase Mind bomb to repress Notch signaling and promote vertebrate neurogenesis
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Epithelial cell polarity is dynamically controlled during early development and is often misregulated in cancer. The serine/threonine kinases PAR-1 and atypical protein kinase C (aPKC) are important players in the establishment of epithelial polarity. Our previous study demonstrated that PAR-1 functions downstream of aPKC to stimulate ciliated cell differentiation in *Xenopus* ectoderm via a Notch signaling-dependent mechanism. Here we show that the same signaling cassette is used during neuronal differentiation of mammalian neural progenitors in vitro. We demonstrate that a crucial molecular substrate for PAR-1 is Mind bomb (MIB), a ubiquitin ligase that promotes Notch signaling by modulating Delta ligand trafficking and activity. The phosphorylation of MIB by PAR-1 results in MIB degradation, repression of Delta-Notch signaling and stimulation of neuronal differentiation. Our data suggest that PAR-1 acts in ectodermal cell fate determination by modulating Notch signaling